



PATENT
Customer No. 22,428
Attorney Docket No. 080618-0237

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: John P. Cooke et al.
Title: Enhancement of Vascular Function by Modulation of
Endogenous Nitric Oxide Production or Activity
Appln. No.: 10/618,835
Filing Date: 07/15/2003
Examiner: J. Russel
Art Unit: 1654

TRANSMITTAL OF INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Transmitted are the following items:

Information Disclosure Statement Under 37 C.F.R. § 1.97 (b) (10 pages);

Form PTO/SB/08 (13 pages);

D. PEARSON and S. SHAW, The Life Extension Companion, Warner Books (1984), NY, pp. cover to
cover (1325 pages total);

Pleadings noted in IDS and cited items therein, as listed in below:

- A. Complaint for Patent Infringement and Demand for Jury Trial (5 pgs.), including:
 - Exhibit A – (12 pgs.)
 - Exhibit B - (27 pgs.);
- B. Answer of Defendant Real Health Laboratories, Inc. to Complaint for Patent Infringement;
and Counterclaim for Declaratory Judgment of Invalidity (11 pgs.);
- C. Plaintiff's Answer to Defendant Real Health Laboratories, Inc.'s Counterclaim for
Declaratory Judgment of Invalidity (4 pgs.);
- D. Second Complaint 02CV 0129 H (John Dullea as an Individual) (12 pgs.), including:
 - Exhibit A (11 pgs.)
 - Exhibit B (14 pgs.)

Exhibit C (4 pgs.)

- E. Plaintiff's Rule 26(a)(1) Initial Disclosures (93 pgs);
- F. Plaintiff's Answers to Defendant's First Set of Interrogatories (12 pgs.), including:
 - Exhibit A (1 pg.)
 - Exhibit B (4 pgs.);
- G. Plaintiff's Responses to Defendant's First Set of Requests for Production of Documents and Things (27 pgs.);
- H. Defendant Real Health Laboratories, Inc.'s Supplemental and Amended Objections and Responses to Plaintiffs Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First set of Requests for Production of Documents and Things (26 pgs.);
- I. Defendant-Counterdefendant Real Health Laboratories, Inc.'s Objections and Responses to Plaintiffs Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First Set of Interrogatories (13 pgs.);
- J. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Supplemental and Amended Objections and Responses to Plaintiffs-Counterdefendants Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First set of Requests for Admission (Nos. 1-39) (14 pgs.)
- K. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Objections and Responses to Plaintiffs-Counterdefendants Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's Second Set of Requests for Admission (Nos. 40-75) (14 pgs.);
- L. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Supplemental and Amended Objections and Responses to Plaintiffs Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First Set of Requests for Production of Documents and Things (Nos. 1-53) (26 pgs.);
- M. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Objections and Responses to Plaintiffs-Counterdefendants Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's 2nd Set of Requests for Production of Documents and Things (Nos. 54-56) (8 pgs.);
- N. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Supplemental and Amended Objections and Responses to Plaintiffs Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First Set of Interrogatories (Nos. 1-11) (13 pgs.);
- O. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Objections and Responses to Plaintiffs-Counterdefendants Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's 2nd Set of Interrogatories (Nos. 12-17, including subparts) (9 pgs.);

- **P.** Defendant-Counterclaimant Real Health Laboratories Lab., Expert Witness Report of Distinguished Professor Alfred Stracher (14 pgs.), including:
 - Exhibit A (8 pgs.)
 - Exhibit B (4 pgs.)
 - Exhibit C (17 pgs.)
 - Exhibit D (5 pgs.);
- **Q.** Defendant-Counterclaimant Real Health Lab. Supplemental and Amended Response to Plaintiffs-Counterdefendants Cooke Pharma, and the Board of Trustees of Leland Stanford Junior University's 2nd Set of Requests for Admission No. 66 (3 pgs.);
- **R.** Defendant-Counterclaimant Real Health Lab. 2nd Supplemental and 2nd Amended Objections and Responses to Plaintiffs Cooke Pharma, and the Board of Trustees of Leland Stanford Junior and 2nd Sets of Interrogatories (Nos. 1-7, 9, 10 and 12-14) (17 pages);
- **S.** Plaintiffs' Third Set of Request for Admission to Defendant Real Health Laboratories, Inc. (4 pgs.);

Tab No.	Document
	Date stamped postcard from application no. 10/060,252, dated 07/10/2003 (1 page);
1	ANB's Joinder in Daily Wellness' Motion for Summary Judgment of Invalidity of the Claims at Issue Under the Doctrine of Inherency (3 pages)
2	Appendix 1 – U.S. Patent 5,217,997, Claim 12 (2 pages)
3	Appendix 1 – U.S. Patent 5,217,997, Claims 9 and 11; Appendix 2 – U.S. Patent 5,428,070, Claims 1 and 3; Appendix 3 – U.S. Patent 5,891,459, Claims 17 and 20; and Appendix 4 – U.S. Patent 6,117,872, Claims 4 and 5 (10 pages)
4	Exhibit K – Palmer et al., "L-Arginine is the Physiological Precursor for the Formation of Nitric Oxide in Endothelium-Dependent Relaxation," <u>Biochem. Biophys. Res. Comm.</u> 153:1251-56 June 1988 (7 pages)
5	Exhibit J – Part 3 – Patent preliminary infringement contentions against defendant Advanced Nutritional Biosystems (15 pages)
6	Exhibit J – Part 2 – Patent preliminary infringement contentions against defendant Daily Wellness (16 pages)
7	Exhibit J – Part 1 – Plaintiff's Disclosure of Asserted Claims and Preliminary Infringement Contentions (10 pages)
8	Exhibit I – The Nobel Prize in Physiology or Medicine 1998, presentation speech (2003) (4 pages)

Tab No.	Document
9	Exhibit H – PDR on-line bookstore “L-Arginine” trade names (8 pages)
10	Exhibit G – The Columbia Encyclopedia, “amino acid” (2001) (2 pages)
11	Exhibit F – U.S. Patent 6,117,872 (15 pages)
12	Exhibit E – U.S. Patent 5,891,459 (27 pages), and Certificate of Correction (1 page);
13	Exhibit D – U.S. Patent 5,428,070 (12 pages)
14	Exhibit C – U.S. Patent 5,217,997 (12 pages)
15	Exhibit B – (manually filed see docket #35)(2 pages)
16	Exhibit A – The Columbia Encyclopedia “arginine” (2 pages)
17	Notice of Motion and Motion for Summary Judgment of Invalidity of the Claims at Issue under the Doctrine of Inherency (19 pages)
18	Declaration of Anup Tikku in Support of Daily Wellness’ Motion for Summary Judgment of Invalidity of the Claims at Issue under the Doctrine of Inherency (3 pages)
19	[Proposed] Order Granting Daily Wellness’ Motion for Summary Judgment of Invalidity (2 pages); and
20	Plaintiff’s List of Proposed Terms and Claim Elements for Construction Pursuant to Patent Local Rule 4-1 (5 pages)

- NAKAKI et al.; “Beneficial Circulatory Effect of L-Arginine”; *Jpn J Pharmacol.*, Vol. 66, (05-23-94), pp. 167-71.
- ITO, THOMAS Y., et al., “A Double-Blind Placebo-Controlled Study of ArginMax, a Nutritional Supplement for Enhancement of Female Sexual Function,” *Journal of Sex & Marital Therapy*, vol. 27, no. 5, October-December, 2001, pp. 541-549.
- SCHACHTER, ALEXANDER, M.D., et al., “Treatment of Oligospermia with the Amino Acid Arginine,” *International Journal of Gynaecology and Obstetrics*, vol. 11, no. 5, 1973, pp. 206-209.
- Derwent Abstract of JP 50048189 A, 04/30/1975, “Fermentative production of L-arginine – in presence of antibiotics, surfactants and antioxidants,” 1 page.
- Derwent Abstract of JP 57005692 A, 01/12/1982, “Fermentative production of L-arginine – by incubation of microorganism of genus *Brevibacterium* or *Corynebacterium*,” 1 page.
- Derwent Abstract of JP 57093913 A, 06/11/1982, “Potentiator for action of spermatozoa – comprises arginine and vitamin-E,” 1 page.

- Derwent Abstract of JP 58055418 A, 04/01/1983, "Hyperlipaemic treatment composition – containing monocolin K and ML-236B carbonate, formed with basic macromolecular compounds, e.g. ion-exchanging polypeptide(s)," 1 page.
- Derwent Abstract of EP 441119 A, 08/14/1991, "Use of L-arginine – to treat high vascular resistance disorders, e.g. hypertension and bronchial asthma," 2 pages.
- Derwent Abstract of EP 511587 A, 11/04/1992, "Slimming beverage- comprises an aminoacid capable of accelerating release of glucagon, a xanthine derivative and thiamine compound in appropriate vehicle," 2 pages.
- Derwent Abstract of EP 511118 A, 10/28/1992, "Use of lysine and arginine pyrrolidone carboxylate(s) as anti-oxidants – preferably with a phenolic derivative, e.g. tocopherol, in pharmaceutical and cosmetic compositions, particularly to protect skin from ageing," 2 pages.
- Derwent Abstract of EP 546796 A, 06/16/1993, "Use of L-arginine – for treating and preventing atherosclerosis," 1 page.
- Inpadoc Abstract of ZA 9410015 A, 11/08/1995, "A pharmaceutical composition," 1 page.
- Derwent Abstract of WO 9318156 A, 09/16/1993, "Endothelial nitric oxide synthase and gene – which catalyses nitric oxide formation, for, e.g., inhibiting platelet aggregation or smooth muscle cell proliferation," 1 page.
- Derwent Abstract of JP 7163269A, 06/27/1995, "Bearing cattle of special gender – by controlling amount of arginine and calcium in feedstuff," 1 page.
- Derwent Abstract of FR 2547501 A, 12/21/1984, "Arginine carbonate, citric acid compositions – giving effervescent agents for tablets, free from alkaline earth metals," 1 page.
- 5,229,390--MORIYAMA et al.-07-20-1993
- 5,352,695--N'GUYEN et al.-10-04-1994

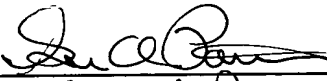
The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

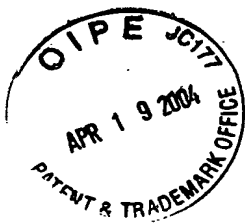
Date 04-19-2004

FOLEY & LARDNER LLP
Customer Number: 22428

Telephone: (202) 672-5569
Facsimile: (202) 672-5399

By  (45,943)
SEAN A. PASSINO
Stephen B. Maebius
Attorney for Applicants
Registration No. 35,264
For

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.



PATENT
Customer No. 22,428
Attorney Docket No. 080618-0237

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: John P. Cooke et al.
Title: Enhancement of Vascular Function by Modulation of
Endogenous Nitric Oxide Production or Activity
Appln. No.: 10/618,835
Filing Date: 07/15/2003
Examiner: J. Russel
Art Unit: 1654

INFORMATION DISCLOSURE STATEMENT
UNDER 37 C.F.R. § 1.97(b)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), Applicants bring to the Examiner's attention the documents on the attached form PTO/SB/08 and pleadings from a litigation concerning parent patents of the present application. This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits for the above-referenced application.

This application is a continuation of U.S. Application No. 10/060,252, filed February 1, 2002, now U.S. Pat. No. 6,646,006, which application is a continuation of U.S. Application 09/930,833, filed August 15, 2001, now abandoned, which application is a continuation of U.S. Application No. 09/075,509, filed May 8, 1998, now U.S. Pat. No. 6,337,321, which application is a continuation of 08/556,035, filed November 9, 1995, now U.S. Pat. No. 5,891,459, which application is a continuation-in-part of U.S. Application No. 08/336,159, filed November 8, 1994, now abandoned,

which application is a continuation-in-part of 08/076,312, filed June 11, 1993, now U.S. Pat. No. 5,428,070.

A. Documents

Copies of the listed documents A1-A229 were previously submitted in prior application no. 10/060,252, filed February 1, 2002, now U.S. Pat. No. 6,646,006, and/or its parents, grandparents, etc., upon which applications Applicants rely for the benefits of 35 U.S.C. §§ 120 and 121.

Copies of documents A204, A224-A225, and A228 are resubmitted.

Copies of documents A230-A241 and B1-B2 are attached.

Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached form.

a. Non-English language documents

JP 50-48189 (04/30/1975) (A48): Attached with this filing is a Derwent Abstract of this document (A230).

JP 57-5692 (01/12/1982) (A49): Attached with this filing is a Derwent Abstract of this document (A231).

JP 57-93913 (06/11/1982) (A50): Attached with this filing is a Derwent Abstract of this document (A232).

JP 58-55418 (04/01/1983) (A51): Attached with this filing is a Derwent Abstract of this document (A233).

JP 3-21786 (01/30/1991) (A53): This document was indicated as considered by the Examiner in the SB/08 of the '252 application.

EP 0511118A1 (L'Oreal) (04/24/1992) (A55): Attached with this filing is a Derwent Abstract of this document (A236). According to the abstract, U.S. Pat. No. 5,352,695 (B2) is in the same family.

JP 7-163269 (06/27/1995) (A59): Attached with this filing is a Derwent Abstract of this document (A240).

FR 2,547,501 (Donzeau) (12/21/1984) (A60): Attached with this filing is a Derwent Abstract of this document (A241).

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in the application and Applicants determine that the cited documents are not "prior art" under United States law, then Applicants reserve the right to present to the Office the relevant facts and law regarding the appropriate status of such documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

B. Litigations

1. Real Health Litigations

The current application is in a family whose patents are involved in litigation. As reported in the an earlier-filed application, both the '459 and the '070 patents were involved in a patent infringement suit in the United States District Court for the Southern District of California (Case No. 01 CV 0854 W). The assignee and exclusive licensee of the '070 and '459 patents, Stanford University and Cooke Pharma, Inc,

respectively, filed a complaint for patent infringement against defendant Real Health Laboratories, Inc. (Real Health) on May 17, 2001. Among other things, Real Health asserted that the '459 and the '070 claims at issue in the civil suit were invalid under 35 U.S.C. §§ 101, 102, 103, and/or 112. The patent infringement suit involving the '459 and the '070 patents was settled before trial, with no decision on the validity of either patent being argued or rendered.

Listed on the accompanying SB/08 forms are references, some of which were produced to counsel for the patentee and used by the defendant in the above-mentioned civil case in its assertion that the claims at issue were invalid.

Also, enclosed and listed herein and in the record of the parent application are copies of pleadings and discovery requests generated in the above-mentioned civil suit which the Office may or may not consider material to patentability of the current application. Once again, the submission of the court-related documents herewith is not intended as an admission that such documents or arguments contained therein are material to patentability.

- A. Complaint for Patent Infringement and Demand for Jury Trial;
- B. Answer of Defendant Real Health Laboratories, Inc. to Complaint for Patent Infringement; and Counterclaim for Declaratory Judgment of Invalidity;
- C. Plaintiff's Answer to Defendant Real Health Laboratories, Inc.'s Counterclaim for Declaratory Judgment of Invalidity;
- D. Second Complaint 02CV 0129 H (John Dullea as an Individual);
- E. Plaintiff's Rule 26(a)(1) Initial Disclosures;
- F. Plaintiff's Answers to Defendant's First Set of Interrogatories;

G. Plaintiff's Responses to Defendant's First Set of Requests for Production of Documents and Things;

H. Defendant Real Health Laboratories, Inc.'s Supplemental and Amended Objections and Responses to Plaintiffs Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First Set of Requests for Production of Documents and Things;

I. Defendant-Counterdefendant Real Health Laboratories, Inc.'s Objections and Responses to Plaintiffs Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First Set of Interrogatories;

J. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Supplemental and Amended Objections and Responses to Plaintiffs-Counterdefendants Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First set of Requests for Admission (Nos. 1-39);

K. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Objections and Responses to Plaintiffs-Counterdefendants Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's Second Set of Requests for Admission (Nos. 40-75);

L. Defendant Real Health Laboratories, Inc.'s Supplemental and Amended Objections and Responses to Plaintiffs Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First Set of Requests for Production of Documents and Things (Nos. 1-53);

M. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Objections and Responses to Plaintiffs-Counterdefendants Cooke Pharma, Inc. and the Board of

Trustees of Leland Stanford Junior University's 2nd Set of Requests for Production of Documents and Things (Nos. 54-56);

N. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Supplemental and Amended Objections and Responses to Plaintiffs Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's First Set of Interrogatories (Nos. 1-11);

O. Defendant-Counterclaimant Real Health Laboratories, Inc.'s Objections and Responses to Plaintiffs-Counterdefendants Cooke Pharma, Inc. and the Board of Trustees of Leland Stanford Junior University's 2nd Set of Interrogatories (Nos. 12-17, including subparts);

P. Defendant-Counterclaimant Real Health Laboratories, Inc.'s, Expert Witness Report of Distinguished Professor Alfred Stracher;

Q. Defendant-Counterclaimant Real Health Laboratories, Inc.'s, Supplemental and Amended Response to Plaintiffs-Counterdefendants Cooke Pharma, and the Board of Trustees of Leland Stanford Junior University's 2nd Set of Requests for Admission No. 66;

R. Defendant-Counterclaimant Real Health Laboratories, Inc.'s, 2nd Supplemental and 2nd Amended Objections and Responses to Plaintiffs Cooke Pharma, and the Board of Trustees of Leland Stanford Junior and 2nd Sets of Interrogatories (Nos. 1-7, 9, 10 and 12-14); and

S. Plaintiff's Third Set of Requests for Admission to Defendant Real Health Laboratories, Inc.

Other pleadings were filed in the file history of the parent case (the '252 application) but are not resubmitted here. These include:

- Real Health's Notice of Motion and Motion to Bifurcate Liability Issues from Damages and to Stay All Proceedings as to Damages; Memorandum in Support of Points and Authorities in Support;
- Memorandum of Points and Authorities in Opposition to Defendant Real Health Laboratories, Inc.'s Motion to Bifurcate Issues from Damages and to Stay all Proceedings as to Damages;
- Declaration of Kenneth S. Klein in Support of Opposition to Defendant Real Health Laboratories, Inc.'s Motion to Bifurcate Issues from Damages and to Stay all Proceedings as to Damages;
- Plaintiff's Notice of Lodgment of Authority taken from an Electronic Database;
- Real Health's Reply in Further Support of its Motion to Bifurcate Liability Issues from Damages and to stay all Proceedings as to Damages, Declaration of Client;
- Order Denying Defendant's Motion to Bifurcate Liability Issues from Damages and to stay all Damages Proceedings;
- Subpoena: Dr. Robert Fried, Ph.D.; and
- Real Health's Notice of Written Disclosure of Expert Witnesses.

Applicants will submit a docket sheet and any document to the Examiner, if the Examiner makes such a request.

2. Daily Wellness and Advanced Nutritional Biosystems Litigations

Also submitted are copies of the Motion for Summary Judgment and related papers filed in a second ongoing litigation against other defendants Daily Wellness and Advanced Nutritional Biosystems (CV 02-05284 in N. Dist. of Cal. San Jose division is representative of the suits). The as-filed papers are listed as follows:

1. ANB's Joinder in Daily Wellness' Motion for Summary Judgment of Invalidity of the Claims at Issue Under the Doctrine of Inherency;
2. Appendix 1 – U.S. Patent 5,217,997, Claim 12;
3. Appendix 1 – U.S. Patent 5,217,997, Claims 9 and 11; Appendix 2 – U.S. Patent 5,428,070, Claims 1 and 3; Appendix 3 – U.S. Patent 5,891,459, Claims 17 and 20; and Appendix 4 – U.S. Patent 6,117,872, Claims 4 and 5;
4. Exhibit K – Palmer et al., "L-Arginine is the Physiological Precursor for the Formation of Nitric Oxide in Endothelium-Dependent Relaxation," Biochem. Biophys. Res. Comm. 153:1251-56 June 1988;
5. Exhibit J – Part 3 – Patent preliminary infringement contentions against defendant Advanced Nutritional Biosystems;
6. Exhibit J – Part 2 – Patent preliminary infringement contentions against defendant Daily Wellness;
7. Exhibit J – Part 1 – Plaintiff's Disclosure of Asserted Claims and Preliminary Infringement Contentions;
8. Exhibit I – The Nobel Prize in Physiology or Medicine 1998, presentation speech (2003);
9. Exhibit H – PDR on-line bookstore "L-Arginine" trade names;
10. Exhibit G – The Columbia Encyclopedia, "amino acid" (2001);
11. Exhibit F – U.S. Patent 6,117,872;
12. Exhibit E – U.S. Patent 5,891,459;
13. Exhibit D – U.S. Patent 5,428,070;
14. Exhibit C – U.S. Patent 5,217,997;
15. Exhibit B – (manually filed, see docket #35);

16. Exhibit A – The Columbia Encyclopedia entry for "arginine;"
17. Notice of Motion and Motion for Summary Judgment of Invalidity of the Claims at Issue under the Doctrine of Inherency;
18. Declaration of Anup Tikku in Support of Daily Wellness' Motion for Summary Judgment of Invalidity of the Claims at Issue under the Doctrine of Inherency; and
19. [Proposed] Order Granting Daily Wellness' Motion for Summary Judgment of Invalidity.

Each item 1-19 was submitted in the '252 application 07-10-2003 and is submitted here again.

The following item is presented for the first time:

20. Plaintiff's List of Proposed Terms and Claim Elements for Construction Pursuant to Patent Local Rule 4-1.

The Examiner is requested to indicate on the record that he considered each item.

a. Motions For Summary Judgment of Patent Invalidity

The Examiner's attention is directed to Items 1 and 17, which contain arguments of unpatentability from each defendant. For example, item 17 at pages 5-6 discusses the "*Life Extension* book," i.e., document A228. According to item 17, the "*Life Extension* book" discloses the compositions that render the patented claims invalid. *Life Extension, supra.* at pp. 461-62; 467-68; 485; 611-13; 620 (see A229). Defendant argued that these compositions formed the basis to invalidate claims of patents in the present application's family. Item 17 at 6-end.

The second defendant, ANB, made arguments in Item 1 and joined with the first defendant's position in Item 17.

The request for attention should not be construed as a representation that any other part of this submission is any less relevant. The Examiner is respectfully requested to consider each submission in its entirety.

Applicants will submit a docket sheet and any document to the Examiner, if the Examiner makes such a request.

CONCLUSION

The Examiner is invited to contact Sean A. Passino (45,943) at (202) 295-4166 if any questions may be resolved by a telephone conference.


The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

Date 04-19-2004

FOLEY & LARDNER LLP
Customer Number: 22428

Telephone: (202) 672-5569
Facsimile: (202) 672-5399

By  (45,943)
SEAN A. PASSINO FOR
Stephen B. Maebius
Attorney for Applicants
Registration No. 35,264

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

Date Submitted: April 19, 2004

(use as many sheets as necessary)

Complete if Known

Application Number	10/618,835
Filing Date	07/15/2003
First Named Inventor	John P. Cooke
Group Art Unit	1654
Examiner Name	J. Russel
Attorney Docket Number	080618-0237

Sheet 1 of 13

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
	A1	2,878,124		KRULKENBERG	03-17-1959	
	A2	3,015,567		HAUSE et al.	01-02-1962	
	A3	3,360,374		BARR, SR. et al.	12-26-1967	
	A4	3,970,750		BROCKEMEYER et al.	07-20-1976	
	A5	4,168,307		OKAMOTO et al.	09-18-1979	
	A6	4,340,592		ADIBI	07-20-1982	
	A7	4,900,566		HOWARD	02-13-1990	
	A8	4,920,098		COTTER et al.	04-24-1990	
	A9	4,957,938		ANDERSON et al.	09-18-1990	
	A10	5,032,377		RADEMACHERS et al.	07-16-1991	
	A11	5,032,608		DUDRICK	07-16-1991	
	A12	5,034,377		ADIBI et al.	07-23-1991	
	A13	5,036,052		OZEKI et al.	07-30-1991	
	A14	5,041,429		SAWAI et al.	08-20-1991	
	A15	5,106,836		CLEMENS et al.	04-21-1992	
	A16	5,157,022		BARBUL	10-20-1992	
	A17	5,171,217		MARCH et al.	12-15-1992	
	A18	5,217,997		LEVERE et al.	06-08-1993	
	A19	5,221,668		HENNINGFIELD et al.	06-22-1993	
	A20	5,248,688		DUDRICK	09-28-1993	
	A21	5,262,435		JOSHUA et al.	11-16-1993	
	A22	5,278,189		RATH et al.	01-11-1994	
	A23	5,288,490		BUDZYNSKI et al.	02-22-1994	
	A24	5,296,246		INOUE et al.	03-22-1994	
	A25	5,326,569		ACOSTA et al.	07-05-1994	
	A26	5,334,617		ULRICH et al.	08-02-1994	
	A27	5,364,644		WALASZEK et al.	11-15-1994	
	A28	5,374,651		KILBOURN et al.	12-20-1994	
	A29	5,380,945		MURAD et al.	01-10-1995	
	A30	5,385,940		MOSKOWITZ	01-31-1995	
	A31	5,428,070		COOKE et al.	06-27-1995	
	A32	5,464,644		WULLSCHLEGER et al.	11-07-1995	
	A33	5,543,430		KAEMMEYER et al.	08-06-1996	
	A34	5,576,287		ZALOGA et al.	11-19-1996	
	A35	5,576,351		YOSHIMURA et al.	11-19-1996	
	A36	5,626,883		PAUL	05-06-1997	
	A37	5,631,031		MEADE	05-20-1997	
	A38	5,650,418		RATH et al.	07-22-1997	
	A39	5,767,160		KAEMMEYER	06-16-1998	
	A40	5,780,039		GREENBERG	07-14-1998	
	A41	5,830,848		HARRISON et al.	11-03-1998	
	A42	5,891,459		COOKE et al.	04-06-1999	
	A43	5,965,529		GARFIELD et al.	10-12-1999	

1158306

Examiner
SignatureDate
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 19, 2004 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
				Attorney Docket Number	080618-0237
Sheet	2	of	13		

U.S. PATENT DOCUMENTS

		U.S. Patent Document				
	A44	5,945,452		COOKE et al.	08-31-1999	
	A45	6,063,432		MAXWELL et al.	05-16-2000	
	A46	6,083,515		GARVEY et al.	07-04-2000	
	A47	5,348,755		ROY	09-20-1994	
	B1	5,229,390		MORIYAMA et al.	07-20-1993	
	B2	5,352,695		N'GUYEN et al.	10-04-1994	

FOREIGN PATENT DOCUMENTS

[illegible]

OTHER – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A61	MERIMEE et al.; "Arginine infusion in maturity-onset diabetes mellitus"; <i>The Lancet</i> (June 11, 1966), pp. 1300-01.	
	A62	DI ROSA; "Azione antiammoniemica ed epatoprotettiva di una associazione a base di pirrolidoncarbossilato di argigina, taurnia e vitamina B ₆ "; <i>Lavoro ricevuto</i> (July 14, 1967).	
	A63	RASK et al.; "Studies on two physiological forms of the human retinol-binding protein differing in Vitamin A and Arginine content"; <i>The Journal of Biological Chemistry</i> ; Vol. 246, No. 21 (November 10, 1971), pp. 6638-46.	
	A64	KADIRVEL et al.; "Uptake of L-Arginine and L-Lysine by the small intestine and its influence on Arginine-Lysine antagonism in chicks"; <i>Journal of Nutrition</i> , Vol. 103, No. 3 (March, 1974), pp. 339-43.	

1158306

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.**

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	10/618,835
Date Submitted: April 19, 2004		Filing Date	07/15/2003
(use as many sheets as necessary)		First Named Inventor	John P. Cooke
		Group Art Unit	1654
		Examiner Name	J. Russel
		Attorney Docket Number	080618-0237
Sheet	3	of	13

OTHER - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A65	BARNES et al.; "The effect of calcium ions on the hydrolysis of benzolarginine ethyl ester by porcine enteropeptidase"; <i>Biochemica et Biophysica Acta</i> ; 452 (1976), pp. 161-64.	
	A66	LECLERCQ-MEYER et al.; "The Role of Calcium in Glucagon Release"; <i>Hormone Res.</i> 7:348-362 (1976).	
	A67	CAMPILLO et al.; "Effect of various concentrations of calcium on Arginine-induced insulin and Glucagon release <i>in vitro</i> "; <i>Revista Espanola de Fisiologica</i> , Vol. 34 (1978), pp. 191-98.	
	A68	BORNHOF et al.; "Hemodynamic splanchnic and renal changes associated with administration of arginine-hydrochloride in dogs"; <i>Res. Exp. Med.</i> (1980) 177:57-70.	
	A69	KECK et al.; "Beeinflussung des Arginininfusions- und Insulin-Toleranz-Tests durch erhöhtes Serumcalcium"; <i>akt. Endokrin.</i> 1:135-142 (1980).	
	A70	FURCHGOTT et al.; "The Obligatory role of endothelial cells in the relaxation of arterial smooth muscle by acetylcholine"; <i>Nature</i> (11-27-1980), pp. 373-76.	
	A71	CALVER et al.; "Dilator actions of arginine in human peripheral vasculature"; <i>Clinical Science</i> (1981) 81:695-700.	
	A72	BARBUL et al.; "Arginine stimulates lymphocyte immune response in healthy human beings"; <i>Surgery</i> (08-1981) 90(2):244-51.	
	A73	BERSON et al.; "A Two Year Trial of Low Protein, Low Arginine Diets or Vitamin B ₆ for Patients with Gyrate Atrophy"; <i>Birth Defects: Original Article Series</i> , Vol. 18, No. 6, pp. 209-218 (1982).	
	A74	KATAN et al.; "Reduction of Casein-induced Hypercholesterolaemia and Atherosclerosis in Rabbits and Rats by Dietary Glycine, Arginine an Alanine"; <i>Elsevier Nothe Holland Scientific Publishers, Ltd.</i> (1982), <i>Atherosclerosis</i> 43:381-91.	
	A75	PEARSON et al.; "Chapter 5: Aging and the Immune System"; <i>Life Extension</i> (1982).	
	A76	BECKEL et al.; "Antioxidative Arginine-Xylose Maillard Reaction Products: Conditions for Synthesis"; <i>Journal of Food Science</i> , Vol. 48 (1983), pp. 996-97.	
	A77	WALLER et al.; "Conditions for the synthesis of antioxidative arginine-xylose maillard reaction products"; <i>Synthesis of Antioxidative Products</i> (1983), pp. 125-40.	
	A78	LEVENSON et al.; "Influence of Supplemental Arginine and Vitamin A on Wound Healing, the Thymus, and Resistance to Infection Following Injury"; <i>Nutritional Support of the Seriously Ill Patient</i> (1983), pp. 53-62.	
	A79	WOOD et al.; "Evidence for Insulin Involvement in Arginine- and Glucose-Induced Hypercalciuria in the Rat"; <i>The Journal of Nutrition</i> , Vol. 113, No. 8 (1983), pp. 1561-67.	
	A80	TANAKA et al.; "Calcium-dependent interactions with calmodulin of a florescent calmodulin antagonist: N ² -dansyl-L-arginine-4-t-butylpiperidine amide"; <i>Archives of Biochemistry and Biophysics</i> , Vol. 220, No. 1 (01-83), pp. 188-92.	
	A81	OLSON et al.; "Avian shell gland contractility: interaction of PGF _{2a} and arginine vasotocin with Ca ²⁺ "; <i>American Journal of Physiology</i> Vol. 244, No. 3 (03-83), pp. C150-57.	

1158306

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Date Submitted: April 19, 2004				Attorney Docket Number	080618-0237
(use as many sheets as necessary)					
Sheet	4	of	13		

OTHER – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A82	HERCHUELZ et al.; "Mechanism of arginine-stimulated Ca ²⁺ influx into pancreatic B cell"; <i>American Journal of Physiology</i> , Vol. 246, No. 1 (01-84), pp. E38-43.	
	A83	DAVRIL et al.; "Arginine Modification in Elastase"; <i>Journal of Biological Chemistry</i> , Vol. 259, No. 6 (03-25-1984), pp. 3851-57	
	A84	BARBUL et al.; "High Arginine levels in Intravenous Hyperalimentation Abrogate Post-Traumatic Immune Suppression"; <i>Journal of Surgical Research</i> (06-1984) 36:620-24.	
	A85	HEISTAD et al.; "Augmented responses to vasoconstrictor stimuli in hypercholesterolemic and atherosclerotic monkeys"; <i>Circulation Research</i> , Vol. 54, No. 6 (06-84), pp. 711-18.	
	A86	PALMER et al.; "Vascular endothelial cells synthesize nitric oxide from L-Arginine"; <i>Nature</i> (06-16-1984) 333:664-66.	
	A87	BARBUL et al.; "Intravenous Hyperalimentation with High Arginine Levels Improves Wound Healing and Immune Function"; <i>Journal of Surgical Research</i> (04-1985) 638:328-34.	
	A88	HOSANG; "Suramin Binds to Platelet-Derived Growth Factor and Inhibits Its Biological Activity"; <i>Journal of Cellular Chemistry</i> (04-30-1985) 29:265-73.	
	A89	WATANABE et al.; "Effects of Vitamin E and Arginine on the Metabolism of Alcohol"; <i>Nutrition Reports International</i> , Vol. 32, No. 1 (07-85), pp. 149-53	
	A90	BARBUL; "Arginine: Biochemistry, Physiology, and Therapeutic Implications"; <i>Journal of Parenteral and Enteral Nutrition</i> (1986) 10(2):227-38.	
	A91	VISEK; "Arginine Needs, Physiological State and Usual Diets. A Reevaluation"; <i>J. of Nutrition</i> (1986) 116:36-46.	
	A92	ROSS; "The Pathogenesis of Atherosclerosis – An Update"; <i>The New England Journal of Medicine</i> , Vol. 311, No. 8 (02-20-86), pp. 488-500.	
	A93	TAKAHARA et al.; "Calcium-dependent Properties of Peptidylarginine Deiminase from Rabbit Skeletal Muscle"; <i>Agric. Biol. Chem.</i> , 50 (11) (06-25-86), pp. 2899-2904.	
	A94	JANSSENS et al.; "Calcium-independent stimulation of glycogenolysis by arginine vasotocin and catecholamines in liver of the axolotl"; <i>J. Endocr.</i> , 109 (1986), pp. 75-84.	
	A95	RIBEIRO et al.; "Pirrolidoncarbossilato Di Arginina E Lisina Nell'Anziano"; <i>Acta Gerontol.</i> 36 fasc. 1-2; 69-76 (1986).	
	A96	FLEMING et al.; "Effects of a phorbol ester and diacylglycerols on secretion of mucin and arginine esterase by rat submandibular gland cells"; <i>Pflügers Arch.</i> , 406 (1986), pp. 6-11.	
	A97	MEYER-LEHNERT et al.; "Atrial Natriuretic Factor (ANF) Inhibits Arginine Vasopressin-Stimulated Ca ²⁺ Fluxes and Cell Contraction in Vascular Smooth Muscle Cells"; <i>Klin Wochenschr</i> 65 (Suppl. VIII) (1987), pp. 115-21.	
	A98	RADOMSKI et al.; "Comparative pharmacology of endothelium-derived relaxing factor, nitric oxide and prostacyclin in platelets"; <i>British J. Pharmac.</i> ; Vol. 92, pp. 181-187 (1987).	

1158306

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Date Submitted: April 19, 2004				Attorney Docket Number	080618-0237
(use as many sheets as necessary)					
Sheet	5	of	13		

OTHER - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A99	HENRIKSON et al.; "Separation and Identification of Two Components of an Estrogen-Responsive, Calcium-Dependent Arginine Esteropeptidase"; <i>J. Steroid Biochem</i> , Vol. 24, No. 2; pp. 189-196 (1987).	
	A100	ANDREWS et al.; "Low-density lipoproteins inhibit endothelium-dependent relaxation in rabbit aorta"; <i>Nature</i> , Vol. 327, 21 (05-87), pp. 237-39.	
	A101	SAITO et al.; "Metabolic and Immune Effects of Dietary Arginine Supplementation After Burn"; <i>Arch. Surgery</i> (07-1987) 122:784-89.	
	A102	JOHANSSON et al.; "The actions of arginine and glucose on glucagon secretion are mediated by opposite effects on cytoplasmic Ca ²⁺ "; <i>Biomedical and Biophysical Research Communications</i> , Vol. 147, No. 1 (08-31-87), pp. 309-14.	
	A103	ISHIKAWA et al.; "Arginine Vasopressin Increases Cellular Free Calcium Concentration and Adenosine 3'-5'-Monophosphate Production in Rat Renal Papillary Collecting Tubule Cells in Culture"; <i>Endocrinology</i> , Vol. 123, No. 3 (1988), pp. 1376-84.	
	A104	PALMER et al.; "Vascular endothelial cells synthesize nitric oxide from L-arginine"; <i>Nature</i> Vol. 333, No. 16 (06-88).	
	A105	YAMAMOTO et al.; "Videomicroscopic Demonstration of Defective Cholinergic Arteriolar Vasodilation in Atherosclerotic Rabbit"; <i>J. Clin. Invest.</i> , Vol. 81, pp. 1752-58 (06-1988).	
	A106	PALMER et al.; <i>Biochem and Biophys Res Comm</i> ; Vol. 153, No. 3, (06-30-88), pp. 1251-56.	
	A107	DALY et al.; "Immune and Metabolic Effects of Arginine in the Surgical Patient"; <i>Ann. Surg.</i> (10-1988) 208(4):512-23	
	A108	PIQUE et al.; "The vasodilator role of endogenous nitric oxide in the rat gastric microcirculation"; <i>European Journal of Pharmacology</i> , Vol. 174 (1989), pp. 293-96.	
	A109	ISHIKAWA et al.; "Effect of ouabain on cellular free calcium and cellular cyclic AMP production in response to arginine vasopressin in rat renal papillary collecting tubule cells in culture"; <i>Journal of Endocrinology</i> , Vol. 121 (1989), pp. 467-77.	
	A110	ELFERINK et al.; "Premeabilization and calcium-dependent activation of rabbit polymorphonuclear leukocytes by poly-L-arginine"; <i>Inflammation</i> , Vol. 13, No. 3 (1989), pp. 285-94.	
	A111	MONCADA et al.; "Biosynthesis of Nitric Oxide from L-arginine"; <i>Biochemical Pharmacology</i> , Vol. 28, No. 11 (1989), pp. 1789-15.	
	A112	IGNARRO; "Endothelium-derived nitric oxide: actions and properties"; <i>FASEB</i> , Vol. 1 (01-89) (ABSTRACT).	
	A113	REES et al.; "Role of endothelium-derived nitric oxide in the regulation of blood pressure"; <i>Proc. Natl. Acad. Sci., USA</i> 86 0 (01-27-1989), pp. 3376-78	
	A114	IGNARRO et al.; "Basic Polyamino Acids Rich in Arginine, Lysine or Ornithine Cause Both Enhancement of and Refractoriness to Formation of Endothelium-Derived Nitric Oxide in Pulmonary Artery and Vein"; <i>Circulation Research</i> , Vol. 64, No. 2 (02-1989), pp. 315-29.	

1158306

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Date Submitted: April 19, 2004				Attorney Docket Number	080618-0237
(use as many sheets as necessary)					
Sheet	6	of	13		

OTHER – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A115	ALBINA et al.; "Regulation of Macrophage Functions by L-Arginine"; <i>J. Exp. Med</i> (03-1989) 169:1021-29.	
	A116	REES et al.; "Role of endothelium-derived nitric oxide in the regulation of blood pressure"; <i>Proc. Natl. Acad. Sci.</i> (05-1989), 86:3375-78.	
	A117	GARG et al.; "Nitric Oxide-generating vasodilators and 8-Bromo-Cyclic Guanosine Monophosphate Inhibit Mitogenesis and Proliferation of Cultured Rat Vascular Smooth Muscle Cells"; <i>J. Clin. Invest.</i> Vol. 83, 1774-77 (05-1989)	
	A118	STAMLER et al.; "N-Acetylcysteine Potentiates Platelet Inhibition by Endothelium-Derived Relaxing Factor"; <i>Circulation Research</i> , Vol. 65, No. 3 (09-1989), pp. 789-95.	
	A119	ALSAKA et al.; "L-Arginine Availability Determines the duration of acetylcholine - induced systemic vasodilatation in vivo"; <i>Biochemical and Biophysical Research Communications</i> (09-15-1989), 163(2) pp. 710-17.	
	A120	MAYER et al.; "Ca ²⁺ -dependent formation of an L-arginine-derived activator of soluble guanylyl cyclase in bovine lung"; <i>FEBS Letters</i> ; Vol. 256, No. 1, 2 (10-89), pp. 211-14.	
	A121	GOLD et al.; Depletion of Arterial L-Arginine Causes Reversible Tolerance to Endothelium-Dependent Relaxation; <i>Biochemical and Biophysical Research Communications</i> (10-31-1989), 164(2): 714-21.	
	A122	POHL et al.; "EDRF Increases Cyclic GMP in Platelets During Passage Through the Coronary Vascular Bed"; <i>Circulation Research</i> , Vol. 65, No. 6 (12-1989), pp. 1798-1803.	
	A123	PIQUE et al.; "The Vasodilator role of endogenous nitric oxide in the rat gastric microcirculation"; <i>European Journal of Pharmacology</i> (12-19-89), 174(2-3): 293-96 (Abstract).	
	A124	MARIN et al.; "Role of Endothelium-Formed Nitric Oxide on Vascular Responses"; <i>General Pharmacology</i> , Vol. 21, No. 5 (1990), pp. 575-87.	
	A125	CARAMELO et al.; "Interaction of arginine vasopressin and angiotensin II on Ca ²⁺ in vascular smooth muscle cells"; <i>Kidney International</i> , Vol. 38 (1990), pp. 47-54.	
	A126	MILYUTINA et al.; "Arginine antiradical and antioxidant effect and its influence on lipid peroxidation during hypoxia"; <i>Biulleten Eksperimentalnoi</i> , Vol. 110, No. 9 (1990), pp. 263-65.	
	A127	MONCADA et al.; "Nitric Oxide From L-Arginine A Bioregulatory system: Chapter 1 – Introduction"; <i>Elsevier Science Publishers B.V.</i> (1990), pp. 1-4.	
	A128	LEVI et al.; "Nitric Oxide From L-Arginine A Bioregulatory system – Chapter 4 – Evidence that L-arginine is the biosynthetic precursor of vascular and cardiac nitric oxide"; <i>Elsevier Science Publishers B.V.</i> (1990), pp. 35-44.	
	A129	SCHRÖDER et al.; "Nitric Oxide From L-Arginine A Bioregulatory system - Chapter 6 - L-Arginine potentiates and N ^G -monomethyl-L-arginine inhibits calcium ionophore-induced cyclic GMP stimulation in porcine aortic endothelial cells," <i>Elsevier Science Publishers B.V.</i> (1990), pp. 55-59.	
	A130	MONCADA et al.; "Nitric Oxide From L-Arginine A Bioregulatory system: Chapter 11 – Endothelium-derived nitric oxide in human arteries and veins," <i>Elsevier Science Publishers B.V.</i> (1990), pp. 89-93.	

1158306

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	
				10/618,835	
				Filing Date	
				07/15/2003	
				First Named Inventor	
Date Submitted: April 19, 2004				John P. Cooke	
(use as many sheets as necessary)				Group Art Unit	
				1654	
				Examiner Name	
				J. Russel	
Sheet 7 of 13				Attorney Docket Number	
				080618-0237	

OTHER – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A131	VALLANCE et al.; "Nitric Oxide From L-Arginine A Bioregulatory system: Chapter 12 – Endothelium-dependent responses and nitric oxide production in human vasculature in vivo"; <i>Elsevier Science Publishers B.V.</i> (1990), pp. 95-99	
	A132	BULT et al.; "Nitric Oxide From L-Arginine A Bioregulatory system: Chapter 13 - Effects of chronic treatment with a source of exogenous nitric oxide on the release of fendothelium-derived relaxing factor by aortae from normal and hypercholesterolaemic rabbits"; <i>Elsevier Science Publishers B.V.</i> (1990), pp. 101-106.	
	A133	JACOBS et al.; "Nitric Oxide From L-Arginine A Bioregulatory system: Chapter 14 – Inhibition of endothelium-derived nitric oxide and atherosclerosis"; <i>Elsevier Science Publishers B.V.</i> (1990), pp. 107-114.	
	A134	COOKE; "Endothelial dysfunction in disease states"; <i>Current Opinion in Cardiology</i> ; Vol. 5, pp. 637-644 (1990).	
	A135	SJOSTRAND et al.; "The effects of L-Arginine and Ng - monomethyl L-Arginine on the inhibitory neurotransmission of the human corpus cavernosum penis"; <i>Acta Physiol Scand</i> (1990), 140:297-98.	
	A136	KUGIYAMA et al.; "Impairment of Endothelium-Dependent Arterial Relaxation by Lysolecithin in Modified Low-density Lipoproteins"; <i>Nature</i> , 344:160-162 (1990).	
	A137	TOMITA et al.; "Rapid and Reversible Inhibition by Low Density Lipoprotein of the Endothelium-Dependent Relaxation to Hemostatic Substances in Porcine Coronary Arteries"; <i>Circulation Research</i> , Vol. 66, No. 1 (01-1990), pp. 18-27.	
	A138	ROČIĆ et al.; "L-arginyl-L-lysine and L-arginyl-L-arginine potentiate the blood glucose-lowering effect of insulin after simultaneous administration in rabbits"; <i>Med. Sci. Res.</i> , Vol. 18; pp. 165-5 (03-01-03-15-90).	
	A139	WEIDINGER et al.; "Persistent Dysfunction of Regenerated Endothelium After Balloon Angioplasty of Rabbit Iliac Artery"; <i>Circulation</i> , Vol. 81, No. 5 (05-1990), pp. 1667-79.	
	A140	DOHI et al.; "Activation of Endothelial L-Arginine Pathway in Resistance Arteries: Effect of Age and Hypertension"; <i>Hypertension</i> (08-90), 15:170-79.	
	A141	NAKAKI et al.; "L-arginine-induced hypertension"; <i>The Lancet</i> (09-15-1990), 336:696.	
	A142	GIRERD et al.; "L-arginine augments endothelium vasodilation in cholesterol-fed rabbits" <i>Circulation Research</i> , Vol. 67, No. 6 (12-1990), pp. 1301-08.	
	A143	MINOR et al.; "Diet induced Atherosclerosis Increases the Release of Nitrogen Oxides from Rabbit Aorta"; <i>J. Clin. Invest.</i> , Vol. 86, 2109-2116 (12-1990)	
	A144	FINEMAN et al.; L-Arginine, a precursor of EDRF in vitro, produces pulmonary vasodilation in lambs"; <i>Am J. Physiol.</i> (1991), 261:H 1563-69.	
	A145	MÜLSCH et al.; "Cytosolic nitric oxide synthesis from L-arginine in mammalian cells"; <i>Progress in Pharmacology and Clinical Pharmacology</i> ; Vol. 8-3 (1991), pp. 73-82.	
	A146	AGOSTONI et al.; "L-Arginine therapy in Raynaud's phenomenon?"; <i>Int. J. Clin. Lab. Res.</i> (1991), 21:202-03.	

1158306

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	10/618,835
		Filing Date	07/15/2003
		First Named Inventor	John P. Cooke
		Group Art Unit	1654
		Examiner Name	J. Russel
Date Submitted: April 19, 2004		Attorney Docket Number	080618-0237
(use as many sheets as necessary)			
Sheet	8	of	13

OTHER - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A147	MILYUTINA et al.; "Antiradical and Antioxidative Effect of Arginine and Its Influence on Lipid Peroxidation Activity During Hypoxia"; Bull. Exp. Biol. And Medicine (1991), 110(9):1198-1200.	
	A148	COOKE et al.; "Arginine restores cholinergic relaxation of hypercholesterolemic rabbit thoracic aorta" (03-1991), <i>Circulation</i> 83(3):1057-62.	
	A149	RUBANYI; "Reversal of Hypercholesterolemia-Induced Endothelial Dysfunction by L-arginine"; <i>Circulation</i> (03-1991), 83(3):1116-20.	
	A150	PARK et al.; "Stimulation of lymphocyte natural cytotoxicity by L-arginine"; <i>The Lancet</i> (03-16-1991), 337:645-46.	
	A151	BATH et al.; "Nitric Oxide and Prostacyclin"; <i>Arteriosclerosis and Thrombosis</i> Vol. 11, No. 2 (03-04-91), pp. 254-60.	
	A152	ROSSITCH et al.; "L-Arginine Normalizes Endothelial Function in Cerebral Vessels from Hypercholesterolemic Rabbits"; <i>J. Clin. Invest.</i> Vol. 87, pp. 1295-1299 (04-91).	
	A153	GOLD; "The effects of calcium, magnesium and L-arginine on biosynthesis of endothelium-derived relaxing factor in bovine pulmonary artery, vein and aortic endothelial cells"; <i>Dissertation Abstracts International</i> ; Vol. 51, No. 10 (04-91), p. 4793-B.	
	A154	SAAVEDRA-MOLINA, et al.; "Stimulation of L-Ornithine Uptake and L-Citrulline and Urea Biosynthesis by D-Arginine"; <i>Biochemistry International</i> Vol. 24, No. 2; pp. 349-358 (05-1991).	
	A155	TANNER et al.; "Oxidized low density lipoproteins inhibit relaxations of porcine coronary arteries"; <i>Circulation</i> ; Vol. 83, No. 6 (06-91), pp. 2012-20.	
	A156	KUBES et al.; "Nitric Oxide: An endogenous modulator of leukocyte adhesion"; <i>Proc. Natl. Acad. Sci.</i> , Vol. 88, pp. 4651-55 (06-1991).	
	A157	KIM et al.; "A Nitric Oxide-like Factor Mediates Nonadrenergic-Noncholinergic Neurogenic Relaxation of Penile Corpus Cavernosum Smooth Muscle"; <i>J. Clin Invest.</i> Vol. 88 (07-1991), pp. 112-18.	
	A158	CALVER et al.; "Dilator actions of arginine in human peripheral vasculature"; <i>Clinical Science</i> (07-10-1991), 81:695-700.	
	A159	MURAKAMI et al.; "Effects of L-arginine on systemic and renal haemodynamics in conscious dogs"; <i>Clinical Science</i> (07-15-1991), 81:727:32.	
	A160	EFRON et al.; "Nitric oxide generation from L-arginine is required for optimal human peripheral blood lymphocyte DNA synthesis"; <i>Surgery</i> (08-1991), 110:327-34.	
	A161	LOPEZ-FARRE et al.; "Inhibition of L-arginine of the Endothelin-Mediated Increase in Cystolic Calcium in Human Neutrophils"; <i>Biochemical and Biophysical Research Communications</i> ; Vol. 178, No. 3 (08-15-91), pp. 884-91.	
	A162	CHEN et al.; "L-Arginine Abrogates Salt-sensitive Hypertension in Dahl-Rapp Rats"; <i>Clinical Investigation</i> (11-1991), 81:1559-67.	
	A163	DREXLER et al.; "Correction of endothelial dysfunction in coronary microcirculation of hypercholesterolaemic patients by L-arginine" (12-21-1991), <i>Lancet</i> 338:1546-50.	

1158306

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 19, 2004 (use as many sheets as necessary)				Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Sheet	9	of	13	Attorney Docket Number	080618-0237

OTHER - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A164	HISHIKAWA et al.; <i>Japanese Heart Journal</i> 33:41-48 (1-1992).	
	A165	HATTON et al.; "Arginine vasopressin mobilised intracellular calcium via V ₁ -receptor activation in astrocytes (pituicytes) cultured from adult rat neural lobes"; <i>Brain research</i> , Vol. 588 (1992), pp. 75-83.	
	A166	BUCHMÜLLER-ROUILLER et al.; "Macrophage activation for intracellular killing as induced by a Ca ²⁺ ionophore"; <i>Biochem J.</i> ; Vol. 264 (1992), pp. 367-92.	
	A167	NARUSE; "Arginine vasopressin increases intracellular calcium ion concentration in isolated mouse collecting tubule cells: Distinct mechanism of action through V ₂ receptor, but independent of adenylate cyclase activation"; <i>Japanese Journal of Nephrology</i> , Vol. 34, No. 4 (1992), pp. 337-47.	
	A168	COOKE; "Endothelium-Derived Factors and Peripheral Vascular Disease"; <i>Cardiovascular Clinics</i> ; Vol. 22, No. 3 (1992), pp. 3-17.	
	A169	LANKIN; "Atherosclerosis as a free radical pathology"; <i>Oxygen Radicals: Proceedings of the 5th International Congress on Oxygen Radicals: Active Oxygen, Lipid Peroxides and Antioxidants</i> , Kyoto (1992) Reed Elsevier Publishers, pp. 385-88.	
	A170	ZEMBOWICZ; "Znaczenie Biologiczne Szlaku Przemian L-Argininy Do Tlenku Azotu"; <i>Folia Medica Cracoviensis</i> ; XXXIII, 1-4 (1992), pp. 103-16.	
	A171	BOEGEHOLD; "Reduced Influence of Nitric Oxide on Arteriolar Tone in Hypertensive Dahl Rats" (1992), Hypertension 19:290-95.	
	A172	VANE et al.; "The Role of Chemical Mediators Released by the Endothelium in the Control of the Cardiovascular System" <i>Int J. Tiss. Reac.</i> XIV (2) (1992), pp. 55-64.	
	A173	RAJFER et al.; "Nitric Oxide as a mediator of relaxation of the corpus cavernosum in response to nonadrenergic neurotransmission"; <i>The New England Journal of Medicine</i> ; Vol. 326, No. 2 (01-09-92), pp. 90-94.	
	A174	JESERICH et al.; "Reduced plasma L-arginine in hypercholesterolaemia"; <i>The Lancet</i> , Vol. 339, (02-29-92), p. 561.	
	A175	MITCHELL et al.; "Native LDL inhibits the release of endothelial derived relaxing factor by reducing the activity of endothelial nitric oxide synthase"; <i>Journal of Vascular Research</i> (02-29-92), p. 169.	
	A176	KUO et al.; "Pathophysiological consequences of atherosclerosis extended into the coronary microcirculation. Restoration of endothelium-dependent response by L-arginine, <i>Circulation Research</i> (03-1992), 70:465-76.	
	A177	HOGAN et al.; "A Cysteine-for-Arginine Substitution (R614C) in the Human Skeletal Muscle Calcium Release Channel Cosegregates with Malignant Hyperthermia"; <i>Anesth Analg</i> 75:441-8 (03-31-92).	
	A178	KANNO et al.; "L-Arginine Infusion Induces Hypotension and Diuresis-natriuresis with Concomitant increased Urinary Excretion of Nitrite-Nitrate and Cyclic GMP in Humans"; <i>Clinical and Experimental Pharmacology and Physiology</i> (04-20-92), 19:619-25.	
	A179	JANSSENS et al.; "Cloning and Expression of a cDNA Encoding Human Endothelium-derived Relaxing Factor-Nitric Oxide Synthase"; <i>The Journal of Biological Chemistry</i> , Vol. 267, No. 21 (07-25-92), pp. 14519-22.	

1158306

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 19, 2004 (use as many sheets as necessary)				Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Sheet	10	of	13	Attorney Docket Number	080618-0237

OTHER – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A180	COOKE et al.; "Antiatherogenic effects of L-arginine in the hypercholesterolemic rabbit; <i>J. Clin. Invest</i> (09-92), 90:1168-72.	
	A181	HARRISON et al.; "Normal and Pathophysiologic Considerations of Endothelial Regulation of Vascular Tone and Their Relevance to Nitrate Therapy"; <i>Am. J. Cardiol</i> (09-24-92), 70:118-78.	
	A182	CREAGER et al.; "L- Arginine Improves Endothelium-dependent Vasodilation in Hypercholesterolemic Humans"; <i>J. Clin. Invest.</i> (10-92), 90:1248-53.	
	A183	IMAIZUMI et al.; "Effects of L-Arginine on Forearm Vessels and Responses to Acetylcholine"; <i>Hypertension</i> , Vol. 20, No. 4 (10-92), pp. 511-17.	
	A184	FUJIHARA; "Effects of Halothane on the Arginine-vasopressin-induced Spatial and Temporal Dynamics of Intracellular Ca ²⁺ Concentration in Single Cultured Smooth Muscle Cells of the Rat Aorta"; <i>Niigata Medical Journal</i> ; Vol. 107, No. 8 (1993), pp. 728-37.	
	A185	SCHINI et al.; "Le monoxide d'azote et l'homeostasie du muscle lisse vasculaire"; <i>Arch Mal Coeur</i> (1993), 86(1): 83-89.	
	A186	MORO et al.; "Activation of adrenal medullary L-arginine: nitric oxide pathway by stimuli which induce the release of catecholamines"; <i>European Journal of Pharmacology – Molecular Pharmacology Section</i> ; Vol. 246 (1993), pp. 213-18.	
	A187	FUJIHARA et al.; "Arginine Vasopressin Increases Perinuclear [Ca ²⁺] in Single Cultured Vascular Smooth Muscle Cells of Rat Aorta"; <i>J. Vasc. Res.</i> , Vol. 30 (1993), pp. 231-38.	
	A188	SUTTON et al.; "Inhibition of voltage-activated Ca ²⁺ currents from cultured sensory neurones by spermine, argitoxin-636 and a synthetic arginine polyamine"; <i>Molecular Neuropharmacology</i> , Vol. 3 (1993), pp. 37-43.	
	A189	KORBUT et al.; "Effect of L-Arginine on Plasminogen-Activator Inhibitor in Hypertensive Patients with Hypercholesterolemia"; <i>New Eng. Journal of Medicine</i> (01-28-93), pp. 328(4):287-88.	
	A190	NUNOKAWA et al.; "Cloning of Inducible Nitric Oxide Synthase in Rat Vascular Smooth Muscle Cells"; <i>Biochemical and Biophysical Research Communications</i> , Vol. 191, No. 1 (02-26-93), pp. 89-99.	
	A191	MILLER et al.; "Determinants of Platelet Intracellular Free Calcium in Essential Hypertension and Effect of Stimulation by Arginine Vasopressin"; <i>American Journal of Hypertension</i> , Vol. 6, No. 3 (03-93), pp. 209-216.	
	A192	WALLACE, "Do Deficiencies of Endothelial Derived Relaxing Factor Contribute to Myocardial Stunning?"; <i>J. Card. Surg.</i> Vol. 8, No. 2 (suppl.) (03-93), pp. 325-28.	
	A193	PANZA et al.; "Effect of Increased Availability of Endothelium-Derived Nitric Oxide Precursor on Endothelium-Dependent Vascular Relaxation in Normal Subjects and in patients with essential Hypertension"; <i>Circulation</i> (05-93), 87: 1475-81.	
	A194	BERDEAUX; "Nitric Oxide: an ubiquitous messenger"; <i>Fundam Clin Pharmacol</i> , Vol. 7 (05-25-93), pp. 401-11.	

1158306

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 19, 2004 (use as many sheets as necessary)				Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Sheet	11	of	13	Attorney Docket Number	080618-0237

OTHER - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A195	McNAMARA et al.; "L-Arginine Inhibits Balloon Catheter-Induced Intimal Hyperplasia"; <i>Biochemical and Biophysical Research Communications</i> ; Vol. 193, No. 1 (05-28-93), pp. 291-96.	
	A196	QI et al.; "Evidence of L-Arginine-Nitric Oxide Pathway in Endothelium and Smooth Muscle of Human Internal Mammary Artery"; <i>Biochemical and Biophysical Research Communications</i> ; Vol. 195, No. 1 (08-31-93), pp. 90-96.	
	A197	MEREDITH et al.; "Role of Endothelium in Ischemic Coronary Syndromes"; <i>Am J Cardiol</i> (09-09-93), 72:27C-32C.	
	A198	CHUA et al.; "Detection of Intraluminal Release of Endothelium-Derived Relaxing Factor From Human Saphenous Veins" (11-93), <i>Circulation</i> 88(pt 2):128-32.	
	A199	MONCADA et al.; "The L-Arginine-Nitric Oxide Pathway; <i>New England Journal of Medicine</i> ; Vol. 329, No. 27 (12-30-93), pp. 2002-12.	
	A200	ZORGNIOTTI et al.; "Effect of large doses of the nitric oxide precursor, L-arginine, on erectile dysfunction"; <i>Int. J. Impotence Res.</i> , Vol. 6 (1994), pp. 33-36.	
	A201	CHIUEH et al.; "The Neurobiology of NO and OH"; <i>The New York Academy Sciences</i> , Vol. 738 (1994), pp. 279-81.	
	A202	HAMON et al.; "Long - Term Oral Administration of L-Arginine Reduces Intimal Thickening and Enhances Neoendothelium-Dependent Acetylcholine-Induced Relaxation After Arterial Injury"; <i>Circulation</i> (1994), 90(3): 1357-62.	
	A203	TSAO et al.; "Enhanced Endothelial Adhesiveness in Hypercholesterolemia is Attenuated by L-arginine"; <i>Circulation</i> , Vol. 89, No. 5 (05-94), pp. 2176-82.	
	A204	NAKAKI et al.; "Beneficial Circulatory Effect of L-Arginine"; <i>Jpn J Pharmacol.</i> , Vol. 66, (05-23-94), pp. 167-71.	
	A205	HIROOKA et al.; "Effects of L-arginine on Impaired Acetylcholine-Induced and Ischemic Vasodilation of the Forearm in Patients With Heart Failure"; <i>Circulation</i> , Vol. 90, No. 2, (08-94), pp. 658-68.	
	A206	HIROOKA et al.; "Effect of L-Arginine on Acetylcholine-Induced Endothelium-Dependent Vasodilation Differs Between the Coronary and Forearm Vasculatures in Humans"; <i>JACC</i> (10-94), 24:948-55.	
	A207	WILLIAMS; "Another vanishing cure?," <i>Alternatives for the Health Conscious Individual</i> (11-94), 5(17): 129-35.	
	A208	WHITAKER (ed.); "An Amino Acid That Could Save Your Life"; <i>Health and Healing; Tomorrow's Medicine Today</i> (11-1994), 4(11):1-8.	
	A209	GILLIGAN et al.; "Contribution of Endothelium-Derived Nitric Oxide to Exercise-Induced Vasodilation"; <i>Circulation</i> (12-1994), 90:2853-58.	
	A210	HECKER et al.; "Mechanisms of Sheer Stress-Dependent Endothelial Nitric Oxide Release: Cardiovascular Implications"; <i>Biochemical, Pharmacological, and clinical aspects of Nitric Oxide</i> (1995), pp. 49-59.	
	A211	BOKELMAN et al.; "Oral L- Arginine Augments Abnormal Endothelium-Dependent Skeletal Muscle Vasodilation in Patients with Coronary Artery Disease"; <i>Circulation</i> (1995), 92(8):1-19.	
	A212	ALBINA et al.; "Chapter 7: Nitric Oxide"; <i>Amino Acid Metabolism and Therapy in Health and Nutritional Disease</i> (1995), pp. 99-115.	

1158306

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 19, 2004 (use as many sheets as necessary)				Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Sheet	12	of	13	Attorney Docket Number	080618-0237

OTHER – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A213	KEYSARY et al.; "The involvement of L-Arginine-Nitric Oxide Pathway in the Anti-Rickettsial Activity of Macrophagelike cells"; <i>Biochemical, Pharmacological, and clinical aspects of Nitric Oxide</i> (1995), pp. 111-14.	
	A214	STARKE; "Streptozotocin chemotherapy in patients with malignant metastatic insulinomas"; <i>Experimental and Clinical Endocrinology & Diabetes</i> , Vol. 103 (2) (1995) (Abstract), p. A53.	
	A215	SINGH; "The effect of intravenous infusion of L-arginine, glycine and D-lysine on urinary calcium excretion in the rat"; <i>Japanese Journal of Physiology</i> , 34, pp. 327-336 (1995).	
	A216	DIPOLO et al.; "Phosphoarginine stimulation of Na ⁺ -Ca ²⁺ exchange in squid axons – a new pathway for metabolic regulation"; <i>Journal of Physiology</i> 487.1; pp. 57-66 (1995).	
	A217	LUGG et al.; "The Role of Nitric Oxide in Erectile Function"; <i>Journal of Andrology</i> (01-1995), 16(1):2-4.	
	A218	GULATI, et al.; "Functional Role of Arginine-11 in the N-terminal Helix of Skeletal Troponin C: Combined Mutagenesis and Molecular Dynamic Investigation," <i>Biochemistry</i> , Vol. 34 (06-06-1995), pp. 7348-55.	
	A219	WHITAKER (ed.); "Advancing Years Need Not Impair Your Sex Life"; <i>Health and Healing; Tomorrow's Medicine Today</i> (09-1995), 5(9) 1,3,5,7.	
	A220	CHEMICAL ABSTRACT 126:190939 (1997), abstracting South Africa Patent No. 9410015, published November 8, 1995.	
	A221	HISHIKAWA, KEIICHI, M.D., et al., "Effect of Systemic L-Arginine Administration on Hemodynamics and Nitric Oxide Release in Man," <i>Japanese Heart Journal</i> , vol. 33, no. 1, January 1992, pp. 41-48.	
	A222	MONCADA, S., et al., "Nitric Oxide: Physiology, Pathophysiology, and Pharmacology," <i>Pharmacological Reviews</i> , vol. 43, no. 2, June 1991, pp. 109-142.	
	A223	GUDE, NM., et al., "Role of endothelium-derived nitric oxide in maintenance of low fetal vascular resistance in placenta," <i>The Lancet</i> , vol. 336, no. 8730, December 22-29, 1990, pp. 1589-1590.	
	A224	SCHACHTER, ALEXANDER, M.D., et al., "Treatment of Oligospermia with the Amino Acid Arginine," <i>International Journal of Gynaecology and Obstetrics</i> , vol. 11, no. 5, 1973, pp. 206-209.	
	A225	ITO, THOMAS Y., et al., "A Double-Blind Placebo-Controlled Study of ArginMax, a Nutritional Supplement for Enhancement of Female Sexual Function," <i>Journal of Sex & Marital Therapy</i> , vol. 27, no. 5, October-December, 2001, pp. 541-549.	
	A226	POLAN, MARY LAKE, M.D. et al., "Clinical Study of ArginMax, a Nutritional Supplement for the Enhancement of Female Sexual Function," <i>Journal of Women's Health & Gender-Based Medicine</i> , vol. 10, no. 4, May 2001, p. 401.	
	A227	HANSEN, JANICE I., M.D., et al., "Clinical Study of ArginMax, a Nutritional Supplement for the Enhancement of Female Sexual Function," <i>Journal of Women's Health & Gender-Based Medicine</i> , vol. 11, no. 3, April 2002. (one page).	

1158306

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 19, 2004 <i>(use as many sheets as necessary)</i>				Application Number	10/618,835
				Filing Date	07/15/2003
				First Named Inventor	John P. Cooke
				Group Art Unit	1654
				Examiner Name	J. Russel
Sheet	13	of	13	Attorney Docket Number	080618-0237

OTHER – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and-or country where published.	T ⁶
	A228	D. PEARSON and S. SHAW, <u>The Life Extension Companion</u> , Warner Books (1984), NY, pp. cover to cover (1325 pages total).	
	A229	D. PEARSON and S. SHAW, <u>The Life Extension Companion</u> , Warner Books (1984), NY, pp. 461-62; 467-68; 485; 611-13; and 620.	
	A230	Derwent Abstract of JP 50048189 A, 04/30/1975, "Fermentative production of L-arginine – in presence of antibiotics, surfactants and antioxidants," 1 page.	
	A231	Derwent Abstract of JP 57005692 A, 01/12/1982, "Fermentative production of L-arginine – by incubation of microorganism of genus Brevibacterium or Corynebacterium," 1 page.	
	A232	Derwent Abstract of JP 57093913 A, 06/11/1982, "Potentiator for action of spermatozoa – comprises arginine and vitamin-E," 1 page.	
	A233	Derwent Abstract of JP 58055418 A, 04/01/1983, "Hyperlipaemic treatment composition – containing monocolin K and ML-236B carbonate, formed with basic macromolecular compounds, e.g. ion-exchanging polypeptide(s)," 1 page.	
	A234	Derwent Abstract of EP 441119 A, 08/14/1991, "Use of L-arginine – to treat high vascular resistance disorders, e.g. hypertension and bronchial asthma," 2 pages.	
	A235	Derwent Abstract of EP 511587 A, 11/04/1992, "Slimming beverage- comprises an aminoacid capable of accelerating release of glucagon, a xanthine derivative and thiamine compound in appropriate vehicle," 2 pages.	
	A236	Derwent Abstract of EP 511118 A, 10/28/1992, "Use of lysine and arginine pyrrolidone carboxylate(s) as anti-oxidants – preferably with a phenolic derivative, e.g. tocopherol, in pharmaceutical and cosmetic compositions, particularly to protect skin from ageing," 2 pages.	
	A237	Derwent Abstract of EP 546796 A, 06/16/1993, "Use of L-arginine – for treating and preventing atherosclerosis," 1 page.	
	A238	Inpadoc Abstract of ZA 9410015 A, 11/08/1995, "A pharmaceutical composition," 1 page.	
	A239	Derwent Abstract of WO 9318156 A, 09/16/1993, "Endothelial nitric oxide synthase and gene – which catalyses nitric oxide formation, for, e.g., inhibiting platelet aggregation or smooth muscle cell proliferation," 1 page.	
	A240	Derwent Abstract of JP 7163269A, 06/27/1995, "Bearing cattle of special gender – by controlling amount of alginine and calcium in feedstuff," 1 page.	
	A241	Derwent Abstract of FR 2547501 A, 12/21/1984, "Arginine carbonate, citric acid compositions – giving effervescent agents for tablets, free from alkaline earth metals," 1 page.	

1158306

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.